Remarks

Claims 1, 12, 13 and 18 are amended in this application. Claims 2, 14 and 15 are canceled. Claim 1, 3-13, 16-20 are pending. No issue of new matter arises.

Claim Amendment:

In view of the Examiner's comments, Applicants respectfully amend the claims for "a method utilizing a double reporter assay for improving signal-to-background ratio to identify an agent which modulates activity of a target molecule, wherein said target molecule affects cellular propagation". The instant invention is targeting on overcoming the disadvantage of these known test systems which usually have relatively low signal-to-background ratio so that their specificity is very low (page 1, lines 22-22). Support for current amendment can be found throughout specification of the instant application, more specifically, in page 10, lines 30-31 and page 19, lines 12-14. Applicants also amend the typographic errors in claims 1, 12, 13 and 18 from "effects" to "affects". The support can be found in the abstract of the instant application. No issue of new matter arises.

Response to Claim objection

Claim 18 has been amended. In claim 18, line 1, "molecules" has been changed to "modulates" as suggested by the Examiner. Allowance of claim 18 is requested upon this amendment.

Response to 35 U.S.C. § 103 rejection

The Examiner rejected claims 1, 3-5, 12-13, 16-17 and 19-20 under 35 U.S.C. § 103 (a) as being unpatentable over Pausch in view of US 6,063,578 and further view of US 20050118690.

The Examiner rejected claims 1, 5, 10-11, and 18 under 35 U.S.C. § 103 (a) as being unpatentable over Crossin et al in view of US 6,063,578 and further view of US 20050118690.

The Examiner also rejected claims 1, 2-11, and 13-14 under 35 U.S.C. § 103 (a) as being unpatentable over Keating et al in view of US 6,063,578 and further view of US 20050118690.

The Examiner states that Pausch (TIBTECH 15: 487-494, 1997, specifically Fig. 1b and p. 490) teaches a method of identifying an agent that modulates the activity of a target molecule by contacting a cell with a candidate compound and modulating a target molecule, Crossin et al (PNAS 94: 2687-2692, 1997, specifically Abstract, Introduction, last paragraph, Expti. Procedures, 2nd , 7th and last paragraph and Figure 4) teach a method of identifying an agent that modulates the activity of a target molecule by contacting a cell and modulating a target molecule, and Keating et al (Oncogene 20: 4281-4290, 2001, specifically Introduction, p. 4282 and Materials & Methods, 1st and 6th paragraphs) teach a method of identifying an agent: that modulates the activity of a target molecule by contacting a cell and modulating a target molecule. However, none of these three references teaches use of two reporters or dual reporter method.

The Examiner further states that US 6,063,578 (specifically columns 8-10) teach a dual reporter assay. Two different reporters need to be used. Enzymatic and fluorescent proteins are taught. It also is stated that the precise reporter genes used are not critical as long as expression can be detected. US 20050118690 (specifically paragraphs 92 and 93) teach a dual reporter assay for isolating transformants. US 20050118690 teaches that it is preferable to have two reporter genes within the cell.

Therefore, the Examiner concludes that the ordinary skilled artisan, desiring to use a dual reporter system, would have been motivated to combine the teachings of Pausch or Crossin et al or Keating et al. with the teachings of US 6,063,578 and US 20050118690 for the claimed invention and, the said skilled artisan would have a reasonable expectation of success in practicing the claimed invention.

Applicants respectfully traverse these rejections.

The key reference cited by the Examiner is US 6,063,578, in which a double reporter gene assay is claimed. However, US 6,063,578 is directed to the objective to provide "a system that permits independent assay of transcription and replication for viral systems" (Column 2, lines 1-4), In other words, it "provides plasmid systems comprising dual reporters for use in the independent evaluation of transcription and replication". With this goal in mind, it specifically states that "the effect of the transcriptional regulator on the second reporter gene should be less than 50% of the effect on the first reporter gene, preferably less than 60%, and more preferably less than 67%." in US 6,063,578 (column 7, lines 42-48).

On the contrary, Applicants apply a double reporter assay in an effort to further increase the measurement window, to multiply the measured signals, and to improve signal-to-background ratio (page 10, lines 27-29 of the instant application) and the double reporter gene assay used in the instant invention consequently improves the signal to approx. 100-150:1 (page 10, lines 30-31 of the instant application). Applicants have demonstrated in the experiments that single growth readout only gave a signal-to-background ratio of approx. 30-50:1 in liquid culture (page 10, lines 23-24 of the instant application).

Therefore, there is no reason to believe that an ordinary skilled artisan would apply the dual reporter system claimed by US 6,063,578, in which the first reporter gene is favored to have minimal effect on the second one, to a method which is aiming to improve signal-to-background ratio by a double reporter assay which the dual reporters improve the readout over the single reporter. Moreover, there is no reasonable expectation of success based on the teachings of the applied art that the measurement window would have been increased by the assay claimed in the instant invention. "Only this combination of growth, a logarithmic event, and the more or less linearly induced expression of measurable enzyme or fluorescent protein leads to the described amplification of the signal, i.e. a large measurement window" (page 11, lines 13-15). This kind of effect could not be expected by an ordinary skilled artisan.

US 20050118690 (specifically paragraphs 92 and 93) teaches a dual reporter

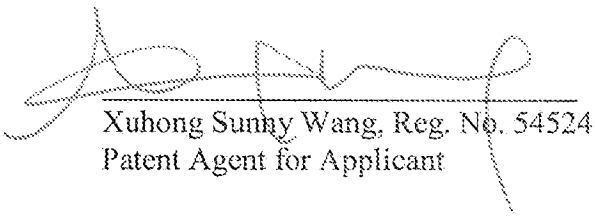
assay for isolating transformants and it is preferable to have two reporter genes within the cell. However, as stated in above argument regarding reference US 6,063,578, US 20050118690 doesn't teach a method with improving signal-to-background ratio and increasing the measurement window. Combining US 20050118690 with US 6,063,578 won't lead to the assay used in the instant invention.

Since neither Pausch nor Crossin et al nor Keating et al teach a double reporter gene method which comprises first step of "contacting a cell with a candidate compound, wherein said cell comprises said target molecule, and wherein said cell further comprises a growth marker reporter gene and a reporter gene selected from the group consisting of a gene coding for an enzyme and a gene coding for a fluorescent protein", and neither US 6,063,578 nor US 20050118690 teaches an assay with improved signal-to-background ratio, either reference alone or the applied references in combination do not teach or suggest every element of the claimed invention (see MPEP § 2143). Furthermore, there are no motivation to combine US 6,063,578 which is directed to the objective to provide "a system that permits independent assay of transcription and replication for viral systems" [emphasis added] to Pausch or Crossin et al or Keating et al for an efficient system which improves signal-to-background ratio and increases the measurement window. And there is no reasonable expectation of success of increasing the measurement window and improving signal-to-background ratio from the teaching of Pausch or Crossin et al or Keating et al. Therefore, the rejections under 35 U.S.C. § 103 are deemed to be improper; withdrawal of these rejections is respectively requested.

The Applicants respectfully submit that claims, as amended, are in condition for allowance, and respectfully request early, favorable action on the application. Should the

Examiner believe that an interview would advance the prosecution of this application, the Applicants invite the Examiner to contact the undersigned at 908.231.3648.

Respectfully submitted,



Xuhong Sunny Wang, Reg. No. 54524
Patent Agent for Applicant

sanofi-aventis U.S. LLC
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807
Telephone (908) 231-**3648**
Telefax (908) 231-2626

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